

Excellence Melting Point Systems

Identification of a Drug Substance

Melting Point of Urea

Conditions

Purpose of the analysis	Determination of the melting range	
Samples	Urea (Caelo pura quality, purity 99.82%)	
Instrument	MP50 Melting Point System	
Glass capillaries	METTLER TOLEDO capillaries, 1.4 mm outside diameter	
Sample preparation	The sample was ground to a powder and filled to a height of 4 mm in capillaries. Adjustment of the fill height and compaction of the powder using the sample preparation tool.	
Temperature program	Start temperature:	128 °C
	Wait time:	10 seconds
	Heating rate:	1 °C/min
	End temperature:	138 °C
Operating mode	Melting range	
Temperature values	Pharmacopeia	

Introduction

The melting point is a criterion used to verify the identity of solid organic substances. According to the European Pharmacopeia (Ph.Eur.) instrumental method, the melting point of a pure substance corresponds to the temperature at which the measured sensor signal reaches its final intensity value. Visually, this is observed as the point at which the last crystal of the substance melts. A pure substance has a sharp melting point, whereas an impure substance melts over a temperature range lower than the melting point of the pure substance (known as melting point depression). This behavior is used to check the purity and identity of the same kind of substances. If a manufacturer's certificate is supplied, the pharmacy only has to check the identity.

In practice, there are two possibilities:

1. Pharmacopeia method: Three determinations according to Ph. Eur. 6.2 2.2.60

Three individual measurements and determination of the mean value. If the instrument used allows you to determine more than one sample, the mean of at least 3 valid results should be determined and compared with the temperature values given by the Pharmacopeia.

2. Your own test method: Determination of the mixed melting point

A small amount of the previously used substance and the new substance are mixed in equal portions. The melting behavior of the mixture and the two individual starting substances is then investigated. If the melting points of all three samples are the same, the starting substances are identical. If the melting points differ, one must assume that the two substances are different or at least contain different amounts of impurities.

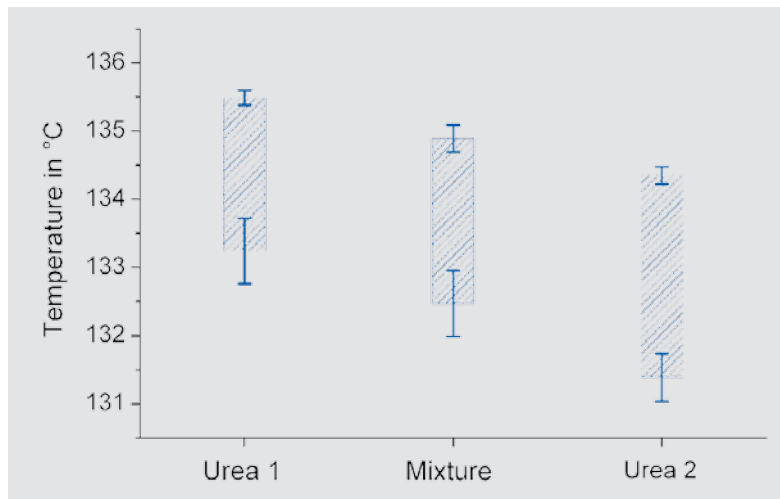
Experimental details

Two substances labeled urea 1 and urea 2, both declared as urea. In the case of urea 1, the melting point of the substance was given as 135 °C. To determine whether the substances were in fact urea, the melting behavior of the individual substances and a 1:1 mixture was investigated using a METTLER TOLEDO MP50 according to the two methods described above. The capillaries were equilibrated isothermally at 128 °C for 10 seconds and then heated at 1 °C/min.

Results

The results are presented in the figure below. They show that the melting ranges of the three samples are different. The melting range of the 1:1 mixture lies between the melting ranges of the two starting substances. This indicates that the two samples are in fact urea. The second sample is however less pure than the first sample. The error bars show the standard deviation of the temperature at the start and end of melting. In each case, it is apparent that the uncertainty of the start of melting is greater than that of the end of melting.

Samples 1 and 2 melt within the temperature range 132 to 135 °C given by the Ph. Eur. This verifies their identity.



Melting ranges of the two urea samples and the 1:1 mixture.

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METTLER TOLEDO
Report
Serial Nr: 5130119610
05/25/2009 09:17:57

Method ID: M9000
Start temp.: 130.0 °C
Rate: 1.0 °C/min
End temp.: 140.0 °C

Analysis comment:
Urea pura Caelo Ch.-B.
70831347 Ph. Eur. 6.2
2.2.60

Results
Number of capillaries: 3
Cap.: 1
Melting point: 135.1 °C
Status: OK
Cap.: 2
Melting point: 135.2 °C
Status: excluded
Cap.: 3
Melting point: 135.0 °C
Status: OK
Cap.: 4
Melting point: 135.1 °C
Status: OK

Melting point
Mean value: 135.08 °C
s: 0.09 °C

Performed by:
Apothekerin Müller
Müller
Signature
  
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Typical printout from the USB-P25 compact printer. It shows a melting point determination in the pharmacopeia mode. Capillary No. 2 was excluded from the mean value calculation.

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For more information

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